International Journal of Current Pharmaceutical Research

ISSN- 0975-7066 Vol 15, Issue 1, 2023

Review Article

DIFFERENT ANALYTICAL TECHNIQUES FOR THE ANALYSIS OF ANTICANCER DRUGS-BOSUTINIB, ENCORAFENIB AND DABRAFENIB-A REVIEW

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Received: 12 Oct 2022, Revised and Accepted: 18 Dec 2022

ABSTRACT

In this present situation there is an increase in the number of diseases has been observed but before this drug come to market, it must undergo several procedures. The validation and analytical methods are the important techniques that help in ensuring its purity and reliability. This process involves the use of various analytical techniques to collect data about the drug. This review includes various types of analytical techniques such as ultraviolet-visible Spectrophotometric and chromatography methods such as high-performance liquid chromatography, hyphenation techniques such as LC-MS for the estimation of selected anti-cancer drugs.

Keywords: Analytical methods, Anti-cancer drugs, Bosutinib, Dabrafenib, Encorafenib

DOI: https://dx.doi.org/10.22159/ijcpr.2023v15i1.2067 Journal homepage: https://innovareacademics.in/journals/index.php/ijcpr

INTRODUCTION

Cancer is an uncontrolled growth of the cancer cells, in which the growth of the normal cell is lost, leading to a solid mass of cells known as tumour or to a liquid cancer (i.e. bone marrow or blood-related cancer) [1]. Cancer affect people at all ages even fetus, which results in lack of ability and differentiation throughout the body. Radiation therapy and chemotherapy are the major clinical treatment which are used for the control of early stages of tumour cells. Nature has a vast variety of useful sources, mainly plants for the discovery and development of drugs against dreadful diseases. Herb is an effective treatment for tumour cells. The drugs derived from medicinal plants are found to be less toxic and side effects [2]. Cancer can be treated by using several chemopreventive agents that they cause toxicity that restrict the usage [3].

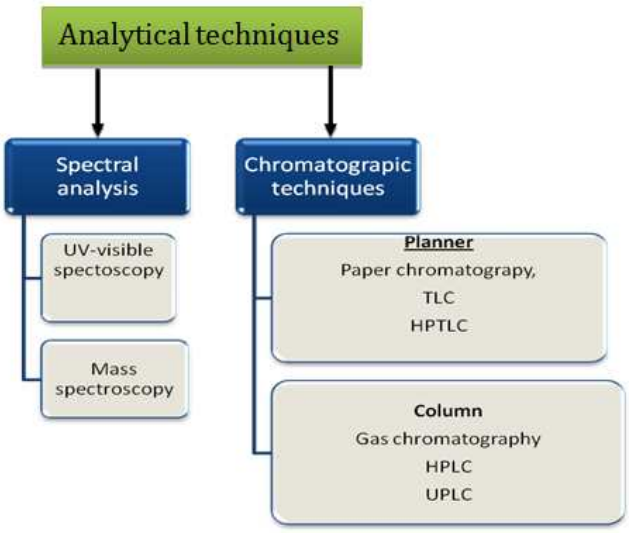

Fig. 1: Schematic representation of analytical techniques

Analytical methods

HPLC

The specific form of column chromatography is high-performance liquid chromatography (high-pressure liquid chromatography) which is used in biochemistry and analysis to separate, identify and quantify active compounds. Pumps in HPLC, are used to pass pressurized liquid solvent, which include a sample mixture to allow it into a column filled with solid adsorbent material. When compared to gas chromatography and capillary electrophoresis, the main limitations of HPLC has long been known to be the lack of high efficiency. One of the most powerful tools in analytical chemistry is HPLC and it is the most accurate analytical methods which is widely used for the quantitative as well as qualitative analysis of drug

product. HPLC is a separation technique which contain mainly mobile phase and stationary phase having opposite polarity equipped with high-pressure pumps and the separation is achieved by the interaction of mobile phase and stationary phase [4-8].

UV spectrophotometric

For analysing multicomponent, UV Spectrophotometric techniques are used for minimizing the cumbersome task of separating interferon's and it is allowed for determining the increasing number of analyte, by consequently reducing the analysis time and cost. Since last 35 y, the most important and advanced analytical instrument in the pharmaceutical industry is ultraviolet spectroscopy. It is based on the method by measuring the absorption of monochromatic light by colourless compounds in the near ultraviolet path of the spectrum (200-400 nm). It is used to determine the identity, strength, quality and purity of such compounds. To perform rapid analysis of multicomponent formulations, biotherapeutic products and samples of a complex matrix, analyst used number of ultraviolet Spectrophotometric methods for these purposes. UV-Visible Spectrophotometry is a favourite tool among all of these methods. Ultraviolet-Visible Spectrophotometers is the instrument which measures the ratio or function of ratio, the intensity of two beams of light in UV-Visible region. Organic compounds can be identified by using a spectrophotometer in qualitative analysis. This technique is simple, rapid, moderately specific and applicable to small quantities of compounds [9-12].

LC-MS/MS

The technique which uses liquid chromatography (or HPLC) with the mass spectrometry is liquid chromatography-mass spectrometry (LC-MS/MS). The most commonly used technique in laboratories for the qualitative and quantitative analysis of drug substances, drug products and biological samples is LC-MS/MS. It played a major role in the evaluation and interpretation of bioavailability, bioequivalence and pharmacokinetic data [13].

Table 1: Different analytical techniques of anti-cancer drugs [14]

S. No.	Drug name	Analytical techniques	Description of techniques	Reference
01	Bosutinib	UPLC-MS/MS	**System:** Acquity ultra-performance liquid chromatography (UPLC) unit **Column:** Acquity BEH C_{18} column (2.1 mm x 50 mm) **Mobile Phase:** ACN**:** 0.1% Formic acid **Flow Rate:** 0.40 ml/min **Run Time:** 3.5 min **Linearity:** 0.1-500 ng/ml. **LOQ:** 0.1ng/ml	[15]
		HPLC	**System:** Shimadzu HPLC LC-2040C 3D Plus with PDA detector **Column**: Cadenza CX-C_{18} column **Mobile Phase: A** 0.5% KH_2PO_4 (pH 3.5): Methanol (80:20) **B** Acetonitrile-methanol (80:20) **Injection Volume:** 20 µl **Flow Rate:** 0.5 ml/min **Wave Length:** 267 nm **Linearity**: 10-500 ng/ml **LLOQ:** 10 ng/ml	[16]
		HPLC-UV	**System:** RP-HPLC with UV detector	[17]
		HPLC	**Mobile Phase:** 0.5% $Na_2PO_4H_2O$ (pH 3.5)-Acetonitrile-Methanol (55:25:20 v/v/v) **Column:** Capcell PAK C_{18}Mg II reversed-phase **Flow Rate:** 1.0 ml/min **UV-Detection:** 250 nm **Linearity Concentration Range:** 25-1500 ng/ml **LOD**: 20 ng/ml **System:** HPLC detector **Mobile Phase:** Methanol: Sodium Phosphate Buffer 10 mm (PH: 6.5, 85:15v/v) **Column:** Primesil C_{18} (Lenght: 250 nm, Diameter: 4.6 nm, Particle Size: 5µ) **Linearity:** 10-50 µg/ml	[17]
		RP-HPLC	**System:** Jasco HPLC–PU 2080 Plus with PDA detector, Software-Borwin-PDA version-1.5 **Column:** Hypersil BDS C_{18} (4.6 X 250mn) 5µm particle size **Mobile Phase:** Methanol: Potassium dihydrogen Phosphate buffer (pH adjusted with OPA to 5.9) **Flow Rate:** 1 ml/min **Wavelenght:** 266 nm **Linearity:** 10-50 µg/ml **LOD**: 0.2 µg/ml **LOQ**: 0.90 µg/ml	[18]
02	Encorafenib	RP-UPLC	**System:** Waters equipped with PDA detector **Column**: HSS C_{18} (100 X 2.1 mm, 1.8 m) **Mobile Phase:** 0.01N KH_2PO_4:Acetonitrile (55:45) **Flow Rate:** 1 ml/min **Wave Length:** 294 nm **Linearity**: 45-270 µg/ml **LOD**: 0.51 µg/ml **LOQ**: 1.55 µg/ml	[19]
		LC-MS/MS	**System:** Agilent 1200 HPLC and an Agilent 6410 QqQ triple quadrupole equipped with ESI **Column:** Hypersil BDS C_{18} **Mobile Phase:** 10 mmol Ammonium formate pH adjusted to 3.8 with Formic acid: Acetonitrile (38:62) **Linear Range:** 5ng/ml to 500ng/ml **Flow Rate:** 0.2 ml/min	[20]

S. No.	Drug name	Analytical techniques	Description of techniques	Reference
			Injection Volume: 2 µl	
		RP-HPLC	**System:** Waters Alliance 2695 with PDA detector, Empower 2 Software **Column:** Agilent C_{18} **Mobile phase:** 0.1M Di Potassium hydrogen phosphate: Methanol (50:50 v/v) **Linearity:** 7.5-22.5µg/ml **LOD:** 0.114µg/ml **LOQ: -**0.381µg/ml	[21]
03	Dabrafenib	UPLC-MS/MS	**System:** Acquity H-class UPLC system, Coupled to a Xevo TQ-S Micro Tandem Mass Spectrometer **Column:** CORTECS UPLC C_{18} Column (2.1× 50 nm, 1.6 µm Particle size, Waters) **Mobile Phase:** 0.1% formic acid and water: ACN **Linearity:** 10-4000 µg/ml **Flow Rate:** 0.8 ml/min **LLOQ:** 10.0µg/ml **HLOQ:** 3999.2µg/ml	[22]
		RP-HPLC	**System:** Water Alliance e2695 HPLC device with 2998 PDA detector **Column:** Symmetry ODS C_{18} (4.6 mm× 150 mm) 5 µm Particle length **Mobile Phase:** Methanol: Zero.1% Orthophosphoric acid (64:36% v/v) **Wave Length:** 224 nm **Linearity:** 20-100µg/ml **LOD:** 0.97 µg/ml **LOQ:** 2.91 µg/ml	[23]
		RP-UPLC	**System:** Water Acquity H-class UPLC System coupled with QSM, Sample Manager and Photodiode array (PDA) detector, Empower PRO 2.0 software **Mobile Phase:** 0.05% Ortho-phosphoric acid in water and methanol **Column:** Acquity BEH C_{18}(100 nm × 2.1 nm, 1.8 µm) **Flow Rate:** 0.3 ml min^{-1} **Injection Volume:** 5 µl **Wave Length:** 225 nm **Linearity:** 12.5 to 125 ng ml^{-1} **LOD:** 12.5ng ml^{-1} **LOQ:** 25ng ml^{-1}	[24]
		LC/MS/MS	**Mass spectrometric detection:** Mode-Multiple reaction mode(MRM) and API5500 (TQ-MS)Triple-quadrupole mass spectrometry positive ion mode, software version 1.5.2 (Sciex) **Mobile Phase:** 10 nm Ammonium bicarbonate in water: methanol **Cloumn:** Gemini C_{18} Column (5.0 µm 50×2.0 mm) **Flow Rate:** 0.250 ml/min **Linearity:** 2.0-200ng/ml **Injection Volume:** 2 µl **LLOQ:** 5; 2ng/ml	[25]

Table 2: Brand names for anticancer drugs

S. No.	Brand name	API	Manufacturing company
01	Bosutris	Bosutinib	Mylan pharmaceuticals
02	Bosulif	Bosutinib	Pfizer Inc
03	Braftovi	Encorafenib	Pfizer Inc
04	Tafinlar	Dabrafenib	Novartis Europharm Limited
05	Rafinlar	Dabrafenib	Novartis Europharm Limited

CONCLUSION

The development and validation of analytical methods plays an essential step for developing any of pharmaceutical products. This review represents that anti-cancer drugs; based on the literature review, it can be concluded that table-1 drugs are performed HPLC, UV, LC-MS for the identification, purification and quantification. Table 2 represents the brand name of individual drugs. The main activity for the analytical development is the separation and characterization of impurities as well as degraded products.

FUNDING

Nil

AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

Declared none

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